Diethylene Glycol Monoethyl Ether

CAS #111-90-0
Swiss CD-1 mice, at 0.0, 0.25, 1.25, or 2.5 %, drinking water
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$CH_3CH_2OCH_2CH_2OCH_2CH_2OH$

Diethylene glycol monoethyl ether (DGEE), a chemical and solvent used in industry and in consumer goods, was tested for reproductive toxicity in Swiss CD-1 mice using the RACB protocol (Williams et al., Fundam Appl Toxicol 14:622–635 [1990]). It was part of a large structure–activity series of glycol ethers and congeners evaluated using this design, generating data on compounds for which there were few or no reproductive data in the open literature. Based on a pilot dose-setting study using food and water consumption, as well as body weight, viability, and clinical signs, doses for the main study were set at 0.0, 0.25, 1.25, and 2.5% DGEE in drinking water for approximately 21 weeks. Based on water consumption data collected during the main study, these concentrations produced calculated DGEE consumptions of approximately 540, 2600, and 5400 mg/kg/day.

In the F_0 mice, there was a nonsignificant (≈10%) weight difference between control and 2.5% DGEE mice by the end of cohabitation. There were no effects on any fertility or reproductive index. Pup indices were unchanged. At the time this study was conducted, the protocol directed that the absence of changes in functional reproductive endpoints meant that the animals were killed without necropsy and discarded; this was the fate of the F_0 mice.

Only the control and high dose levels were evaluated for the second generation. DGEE had no effect on the viability or weight gain in the F_1s as they matured. In the single mating trial for this generation, there were no treatment-related differences in pup number or weight or viability. Necropsy of the F_1 mice as adults revealed no change in body weight, but a 12% increase in liver weight and a 6% decrease in brain weight in both males and females. There was a 34% reduction in the percent of sperm that were motile in the treated males, with no other change in sperm indices.

In summary, 2.5% DGEE is a weak reproductive toxicant in male Swiss CD-1 mice, based on the reductions in sperm count seen in the second generation. It is not a selective reproductive toxicant, as sperm counts were reduced at doses that also increased liver weight.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85137123**
Chemical: **Diethylene Glycol Monoethyl Ether**
CAS#: **111-90-0**
Mode of exposure: **Drinking water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.25%	1.25%	2.5%
General toxicity	Male, female	Male, female	Male, female
Body weight	•	•	•
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	•	•	•
Feed consumption	•	•	•
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	— , —	— , —	— , —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	—	—

F_1 generation — Dose concentration →	•	•	2.5%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	•
Mortality	•	•	•
Adult body weight	•	•	— , —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	↑ , ↑
Feed consumption	•	•	•
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	— , —
Absolute testis, epididymis weight[a]	•	•	— , —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	— , —
Epidid. sperm parameters (#, motility, morphology)	•	•	↓ , — , —
Estrous cycle length	•	•	•

Summary information	
Affected sex?	**Unclear**
Study confounders:	**None**
NOAEL reproductive toxicity:	**1.25%**
F_1 more sensitive than F_0?	**Unclear**
Postnatal toxicity:	**Unclear**

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); — , —, no change in males or females. [a]Adjusted for body weight.